IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 9517**
Tsuyoshi SUZUKI et al.	:	Attorney Docket No. 2004_1909A
Serial No. 10/516,360	:	Group Art Unit 1625
Filed March 4, 2005	:	Examiner Taofiq A. Solola
PREVENTIVES AND/OR REMEDIES FOR SUBJECTS WITH THE EXPRESSION OR ACTIVATION OF Her2 AND/OR EGFR	:	**Mail Stop: AMENDMENT**

SUPPLEMENTAL REPLY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Attached to this paper is a Declaration by Tsuyoshi Suzuki, executed June 27, 2008. This Declaration is the original, a copy of this Declaration was submitted with our response to the Office Action of April 3, 2008. Please replace the copy Declaration with this attached Declaration.

Respectfully submitted,

Tsuyoshi SUZUKI et al.

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July 10, 2008

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

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DECLARATION UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents,
Washington, D.C.

Sir:

I, Tsuyoshi Suzuki, the undersigned, a citizen of Japan, residing at 2-30-40 Sumiyoshi, Fuchu, Tokyo do hereby declare:

1. That I am an inventor of the above-identified application.

2. That I graduated from Tohoku University, graduate school of pharmaceutical science with a Master's degree in 1992.

3. I am an employee of Mitsubishi Tanabe Pharma Corporation. I have joined the company and been doing research of anticancer agents since 1992.

4. Relevant Publication: Suzuki T, Fujii A, Ohya J et al. Pharmacological characterization of MP-412 (AV-412), a dual epidermal growth factor receptor and ErbB2 tyrosine kinase inhibitor. Cancer Science 2007; 98: 1977-1984.

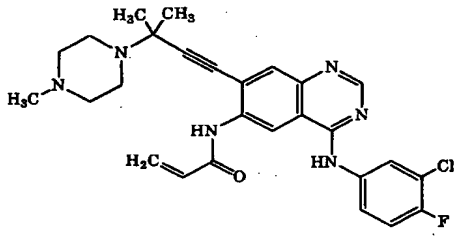
5. That in order to show enablement under 35 U.S.C. § 112 of Claims 19-24 of the above-identified application, I have under my control and direction conducted the following experiments. The particulars and results of the experiments are set forth hereinbelow.

EXPERIMENTAL DATA

1. Object: *In vivo* antitumor effects

2. Method: Antitumor effects of compound A were evaluated by using various human cancer cell lines which express Her2 and/or EGFR. Human lung cancer NCI-H1975 (ATCC No. CRL-5908), prostate cancer DU145 (ATCC No. HTB-81) and ovarian cancer SKOV-3 (ATCC No. HTB-77) were purchased from ATCC. Human esophageal cancer TE-8 was obtained from the Cell Resource Center for Biomedical Research (Tohoku University). Human Breast cancer KPL-4 was gift from Dr. Junichi Kurebayashi (Kawasaki Medical University). The chemical name and the structure of compound A are as follows.

N-{4-[(3-Chloro-4-fluorophenyl)amino]-7-[3-methyl-3-(4-methyl1-piperazinyl)-1-butynyl]-6-quinazolinyl}acrylamide



3. Results: The results are shown in the following Tables.

(Table x1)

Antitumor effects on human lung cancer NCI-H1975 (both EGFR, Her2 positive)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	5.5	100
Compound A· 2TsOH	75	3.1	47
Compound A· 2TsOH	150	0.9	-2

(Table x2)

Antitumor effects on human breast cancer KPL-4 (both EGFR, Her2 positive)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	4.8	100
Compound A·2TsOH	100	1.5	14

(Table x3)

Antitumor effects on human prostate cancer DU145 (both EGFR, Her2 positive)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	3.3	100
Compound A·2TsOH	100	1.3	11

(Table x4)

Antitumor effects on human ovarian cancer SKOV-3 (both EGFR, Her2 positive)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	9.6	100
Compound A·2TsOH	100	6.1	60

(Table x5)

Antitumor effects on human esophageal cancer TE-8 (both EGFR, Her2 positive)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	5.6	100
Compound A·2TsOH	10	0.34	-14

(Table x6)

Antitumor effects on human pancreatic cancer HPAC (both EGFR, Her2 positive)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	6.6	100
Compound A·2TsOH	100	2.9	33

(Table x7)

Antitumor effects on human cervical cancer ME-180 (EGFR positive, Her2 negative)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	9.6	100
Compound A·2TsOH	100	6.1	60

(Table x8)

Antitumor effects on human colorectal cancer LS174T (EGFR negative, Her2 positive)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	13.9	100
Compound A·2TsOH	100	8.2	56

(Table x9)

Antitumor effects on human lung cancer NCI-H520 (both EGFR, Her2 negative)			
Pharmaceutical agent	Dose mg/kg	Average relative tumor growth rate	% control
Control	-	7.4	100
Compound A·2TsOH	100	6.5	86

5. Conclusion: From the results shown above in the tables, it is my expert opinion and belief that compound A suppresses the growth of various human cancer types which possess Her2 and/or EGFR. Thus, it is my expert opinion and belief that the claimed invention is enabled.

I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date: June 27, 2008

Tsuyoshi Suzuki

(Signature of Declarant)